

Cefuroxime in pediatric practice*

COMMITTEE ON INFECTIOUS
DISEASES AND IMMUNIZATION,†
CANADIAN PAEDIATRIC SOCIETY

Cefuroxime (Zinacef) is a second-generation cephalosporin antibiotic that has recently been licensed in Canada for parenteral use; it has been available in Europe for several years. Like other cephalosporins, its antibacterial activity results from the inhibition of cell wall synthesis.¹

Most of the extensive information available on the clinical use of cefuroxime is derived from clinical trials in adults.¹⁻³ Licensed indications in-

clude the treatment of lower respiratory tract, urinary tract and soft tissue infections caused by susceptible organisms. Cefuroxime has been used in life-threatening infections, including meningitis, sepsis and osteomyelitis, when the initial therapy had been unsuccessful. In vitro it is active against *Haemophilus influenzae* (including strains resistant to ampicillin), *Escherichia coli*, *Proteus mirabilis*, *Enterobacter* sp. and *Klebsiella* sp. Cefuroxime's activity against *Staphylococcus aureus* is maintained whether the strain produces penicillinase or not; however, methicillin-resistant strains are also resistant to cefuroxime. Most strains of *Neisseria meningitidis*, *N. gonorrhoeae*, *Streptococcus pneumoniae* and other streptococcal species are very sensitive to cefuroxime. However, *Strep. faecalis* (enterococcus) and *Pseudomonas aeruginosa* are resistant. *Listeria monocytogenes* is also resistant to cefuroxime, as it is to other cephalosporin-like antibiotics. Therefore, cefuroxime should never be used alone when *Listeria*, *Pseudomonas* or enterococci are possible causes of an infection. Cefuroxime is active against oral anaerobes and *Clostridium*, but most isolates of *Bacteroides fragilis* are resistant.

Cefuroxime is not metabolized to any extent in vivo and is excreted almost entirely by the kidneys. The serum half-life, usually 1.5 hours, is prolonged to 20 hours in anuric patients. Dosing intervals must be adjusted if the creatinine clearance is low. The drug's diffusion into soft tissues is excellent.³ Its penetration into the cerebrospinal fluid is usually good (the levels reaching about 40% of serum levels) if the meninges are inflamed. Although one prospec-

tive randomized trial suggested that cefuroxime was equivalent to ampicillin and chloramphenicol for the treatment of meningitis,⁴ experience with its use in children is limited, and cefuroxime is not recommended as a first-line drug for meningitis.

Adverse effects

The side effects encountered include all those typical of cephalosporins — rash, fever, eosinophilia, and thrombophlebitis or inflammation at the injection site — but have been infrequent.^{2,3} Bleeding, a problem in some recipients of cefamandole and certain other new cephalosporins, has not been described with cefuroxime. Reactions can be anticipated in patients allergic to other cephalosporins.

Dosages

The most appropriate daily dosage for children has yet to be determined,⁵⁻⁸ but 30 mg/kg is recommended for urinary tract infections, 75 to 100 mg/kg for soft tissue infections or sepsis and 200 to 240 mg/kg for meningitis. The drug should be administered at 6- to 8-hour intervals. A daily dosage of 50 mg/kg, divided into two doses, has been recommended for infants in their first week of life.^{6,9}

Conclusions

The role that cefuroxime may play in the treatment of common pediatric infections is not fully determined.¹⁰ Cefuroxime penetrates more readily into soft tissue, urine and cerebrospinal fluid than does cefamandole, another second-generation cephalosporin. It should be

*This article is the second of four statements prepared by the committee that are appearing in consecutive issues of the Journal.

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ONCE A DAY
'VIBRAMYCIN'
(DOXYCYCLINE/PFIZER)

Classic Therapy
In Bronchitis and Sinusitis

Prescribing Information

ACTION

Vibramycin is a broad spectrum antibiotic and is active against a wide range of gram-negative and gram-positive organisms. Vibramycin exerts its antimicrobial effect by inhibition of protein synthesis. There is evidence to suggest that oral Vibramycin, because of its rapid and almost complete absorption, may have less effect on the gut flora than other tetracyclines. Hinton (1968) has reported that the normal dosage regimen of tetracycline HCl administered to 17 volunteers was associated with important effects on the intestinal flora in terms of both changes in total population and the emergence of resistant strains. Large doses of oral Vibramycin (double the maximum recommended dosage) had to be administered to produce an equivalent effect. In a similar number of volunteers, however, administration of the normal dosage regimen of oral Vibramycin was associated with substantially less effect on gut flora. Barteaux (1968) noted that the gut flora of patients on various dosages of oral Vibramycin for 10-80 days showed no significant deviation from the normal flora or from the flora of a control group of patients. These data suggest that microbiological intestinal complications (e.g., diarrhea) associated with tetracycline therapy may be less frequent when ordinary therapeutic doses of doxycycline are used.

INDICATIONS AND CLINICAL USE

Oral Vibramycin is indicated for the treatment of respiratory infections such as single and multilobe pneumonia, broncho-pneumonia, bronchitis, sinusitis, pharyngitis, tonsillitis, and otitis media caused by susceptible strains of *β*-hemolytic *Streptococcus*, *Staphylococcus*, *Pneumococcus*, *H. influenzae*, *Klebsiella pneumoniae* and *Mycoplasma pneumoniae*.

CONTRAINDICATIONS

Vibramycin is contraindicated in individuals who have shown hypersensitivity to tetracyclines.

WARNINGS

As with other tetracyclines, Vibramycin may form a stable calcium complex in any bone-forming tissue, though *in vitro* it binds calcium less strongly than other tetracyclines. Though not observed in clinical studies to date, it should be anticipated that like other tetracyclines the use of Vibramycin during tooth development (last trimester of pregnancy, during lactation, neonatal period and early childhood) may cause discoloration of the teeth. Though more commonly associated with long-term use of tetracyclines, this effect has also been known to occur after short courses.

PRECAUTIONS

In clinical studies to date, Vibramycin administration did not lead to increased serum levels nor to an increase in the serum half-life of doxycycline in patients with impaired renal function. Vibramycin in normal dosage may be used to treat these patients. Although no evidence of increased toxicity has been observed in such patients, the potential for increased hepatic or other toxicity should be considered until further data on the metabolic fate of doxycycline under these conditions become available. Liver function tests should be carried out at regular intervals on patients receiving high doses for prolonged periods of time. Concurrent administration of Vibramycin and agents known to be hepatotoxic should be avoided if possible. The use of antibiotics may occasionally result in overgrowth of non-susceptible organisms; thus, observation of the patient is essential. There is evidence to suggest that Vibramycin, may have less effect on the gut flora than other tetracyclines. Vibramycin should not be administered

to pregnant and lactating women or neonates until its safety in such cases has been established beyond all reasonable doubt, unless in the judgment of the physician the potential benefit to the patient outweighs the risk to the fetus or child. Certain hypersensitive individuals may develop a photodynamic reaction to sunlight during treatment with Vibramycin. If this or any other allergic reaction should occur, medication should be discontinued. Increased intracranial pressure with bulging fontanelles has been observed in infants receiving therapeutic doses of tetracycline. Although the mechanism of this phenomenon is unknown, the signs and symptoms have disappeared rapidly upon cessation of treatment with no sequelae.

ADVERSE REACTIONS

As with other broad-spectrum antibiotics, gastrointestinal disturbances such as nausea, vomiting and diarrhea, as well as glossitis, stomatitis and proctitis may occur, but have rarely been sufficiently troublesome to warrant discontinuation of therapy. As with other tetracyclines, elevation of SGOT or SGPT values, anemia, neutropenia, eosinophilia, leukopenia or elevated BUN has been reported, the significance of which is not known.

SYMPTOMS and TREATMENT OF OVERDOSAGE

Gastric lavage if necessary.

DOSAGE AND ADMINISTRATION

The recommended dosage of oral Vibramycin in adults for the majority of susceptible infections is a single loading dose of 200 mg on the first day of treatment followed by a maintenance dosage of 100 mg once daily at the same time each day thereafter. The recommended dosage schedule for children over one month weighing up to 50 kg is a single loading dose of 5 mg/kg of body weight on the first day, followed by a maintenance dosage of 2.5 mg/kg once daily at the same time each day thereafter. As absorption is not significantly affected by food or milk, Vibramycin should be given with or after a meal thus minimizing the possibility of gastric upset. Antacids and iron preparations impair absorption and should not be given concomitantly to patients taking oral Vibramycin. In severe infections in adults, such as lung abscesses or osteomyelitis, and in chronic urinary tract infections, a single daily dose of 200 mg may be used throughout. For more severe infections in children, up to 5 mg/kg of body weight may be given. Therapy should be continued after symptoms and fever have subsided. It should be noted, however, that effective antibacterial levels are usually present 24 to 36 hours following discontinuance of Vibramycin therapy. When used in streptococcal infections, therapy should be continued for 10 days to prevent the development of rheumatic fever or glomerulonephritis. No alteration in recommended dosage schedule need be made when treating patients with impaired renal function.

DOSAGE FORMS

Vibramycin capsules are available as 100 mg (blue) hard gelatin capsules containing doxycycline hyclate equivalent to 100 mg of doxycycline, supplied in bottles of 50 and 200. Vibramycin for oral suspension (doxycycline monohydrate) is available as a dry powder for oral suspension containing, when reconstituted, doxycycline monohydrate equivalent to 25 mg of doxycycline/5 mL (each teaspoonful) with a pleasant raspberry flavor in 50 mL bottles.

Reference

1. Cunha, Burke A., M.D., Respiratory Infections: An Appraisal of the Role of Doxycycline, Postgraduate Medicine Communications, Special Report, September 1979.

useful in treating infections that may be caused by *H. influenzae* type b, such as facial cellulitis, epiglottitis, pneumonia and septic arthritis, and it would then replace chloramphenicol. Unlike cefamandole, cefuroxime retains its activity in the presence of large inocula of β -lactamase-producing *H. influenzae*; therapeutic failures have not been reported. Because of the high concentration achieved in the urine, cefuroxime should be an excellent antibiotic for the treatment of urinary tract infections caused by susceptible organisms. Experience in the treatment of meningitis, however, is limited, and in Canada the drug is not licensed for this indication. The cost of the drug is similar to that of cefamandole.

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